Non-Technical Abstract

Cholera is a disease caused by infection with bacteria called *Vibrio cholerae*. Very few cases of cholera are seen in the United States. Large outbreaks of cholera have occurred in Asia, Africa, and South America. The main symptom of cholera is watery diarrhea. The watery diarrhea can be so severe that even adults can become dehydrated, go into shock, and die if they are not treated. Cholera diarrhea is caused when a toxin (poison) is made by *Vibrio cholerae* bacteria. This poison acts on the lining of the intestine and causes an increased amount of water in the intestine. This increased water in the intestine becomes diarrhea, which may be very watery and in large amounts. Other symptoms of cholera include low grade fever, stomach cramps, nausea, vomiting, and loss of energy.

The currently available licensed cholera vaccine is not effective and is no longer recommended. New, more effective cholera vaccines are needed to prevent cholera. To develop new vaccines, more information is needed about the bacteria *Vibrio cholerae* and how it causes diarrhea. One new vaccine, CVD 103 HgR, consists of the bacteria *Vibrio cholerae* from which the toxin has been removed by genetic engineering. However, this vaccine still causes mild diarrhea in volunteers, even though it does not have the toxin. Scientists think that *Vibrio cholerae* may make other toxins or other proteins when it is inside the human body that cannot be detected in the laboratory. If these toxins or other proteins could be identified, then they could be removed from the bacteria. This would result in a safer vaccine. After infection with *Vibrio cholerae* or after vaccination against cholera, a number of proteins called antibodies are made in the body. These antibodies fight cholera proteins and help prevent diarrhea. Scientists don't know which cholera proteins these antibodies fight. If they did, this would also help scientists design a better cholera vaccine.

The study will be conducted on a research isolation ward, where 3-5 volunteers will be given live *Vibrio cholerae* bacteria to drink. The *Vibrio* have been specially treated using genetic engineering. As a result, the *Vibrio* no longer make cholera toxin. In addition, the proteins that are made by the bacteria inside the body will be labeled. This means that the labeled proteins can be identified in the laboratory. The *Vibrio* bacteria will live and grow inside the volunteers'intestine for a few days. The *Vibrio* bacteria will come out of the body with the volunteers'stools. We will save the stools and culture them in the laboratory to see which proteins have the special label. The proteins with the label are the ones that the bacteria produced in the intestine. Blood samples will also be collected to look for specific antibodies against *Vibrio*. Intestinal fluid will be obtained by swallowing a gelatin string capsule one and two days after swallowing the cholera bacteria. The purpose of this is to see if bacteria can be found in the upper part of your small intestine. Four days after swallowing the cholera bacteria (or earlier, if you develop severe symptoms), volunteers will be given tetracycline tablets to take by mouth for 5 days to remove the bacteria from your intestine. Results from this study may be used to develop a more effective and safer vaccine.